Remarks/Arguments:

These remarks are responsive to the Final Office Action of December 10, 2008. The rejections of claims 1 and 3 over Sharma under 35 USC Section 102(a) have been withdrawn. Claim 38 has been cancelled and new claim 39 is added. Support for claim 39 is found in the published specification, US 2007/0092489, at paragraph [0041]. No new matter is added by these amendments.

Claim 33 stands rejected under 35 USC Section 112 as indefinite. Claim 33 has been corrected to overcome this rejection. Applicants therefore request that the rejection of claim 33 for indefiniteness be withdrawn.

Claims 1, 3, 8, 10, 33, and 38 stand rejected under 35 USC 102(b) as anticipated by Halbreich (US 6,150,181). Claim 38 is cancelled. The Office Action states that Halbreich teaches nanoparticles composed of magnetite Fe_3O_5 and maghemite γFe_2O_3, and that these compounds can be reasonably interpreted to be "metals," but the Office Action provides no evidentiary support for this interpretation.

Applicants traverse this rejection. Iron oxide compounds are not considered "metals" by those of skill in the art.

The American Heritage Science Dictionary defines "metals" as follows:

> (1) Any of a large group of chemical elements, including iron, gold, copper, lead, and magnesium, that readily become **cations** and form **ionic bonds**, having relatively free **valence electrons** (electrons in the outer shells). Metals are generally good conductors of electricity because of the freedom of their valence electrons. Metals generally conduct heat well, and in solid form are relatively malleable and ductile compared to other solids. They are usually shiny and opaque. All metals except mercury are solid at room temperature.
>
> (2) An alloy, such as steel or bronze, made of two or more metals.

http://dictionary.reference.com/browse/metals#dict_header.

Metal oxide compounds such as magnetite and maghemite are not encompassed by this definition. However, if this is nonetheless the Examiner's meaning, Applicants request that the Examiner provide an affidavit or declaration to support Official Notice of this contention, including citation to some authority to provide sound technical reasoning for the assertion, as required by MPEP Section 2144.03C.

Claims 1, 8-10, 33, and 38 stand rejected under 35 USC Section 102(b) as anticipated by Feijen (US 4,634,762). Claim 38 is cancelled. The Office Action states that Feijen teaches covalently bonded conjugates of an anticoagulant and protein which are coupled via amide linkages and also teaches that these conjugates may be used with "a surgical apparatus (which inherently reads on the metal surface of a medical device recited in claim 8)," Office Action, page 7. Applicants traverse this rejection for the following reasons.

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" MPEP Section 2112 IV quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP Section 2131 quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

A metal surface is not "necessarily present" in the term "surgical apparatus," as the surgical apparati may also be composed of nonmetals such as plastics, teflon, fibers, *etc.* For this reason, a metal surface is not inherent in the term "surgical apparatus." Accordingly, Feijen does not disclose every limitation of Applicants' claims and does not anticipate Applicants' claims.

In addition, Feijen teaches covalent bonding of heparin to a protein, but does not teach covalent bonding of heparin or a protein, or the heparin-protein complex to a metal surface or to any surface either directly or through a cross-linking compound. Feijen, in contrast, teaches adsorption of the heparin-protein complex to a surface. Applicants' claims are directed to the covalent bonding of a modified protein to a metal surface, as discussed further below, and are not directed to adsorption of a protein to a surface. Therefore, Feijen does not disclose every limitation of Applicants' claims and cannot anticipate claims 1, 8-10, or 33. Accordingly, Applicants request that the rejection of these claims over Feijen under Section 102(b) be withdrawn.

Claims 1, 8-10, 33 and 38 stand rejected under 35 USC 102(e) as anticipated by Kutryk (US 7,037,332). Claim 38 is cancelled. The Office Action states that Kutryk discloses a medical device coated with antibodies and a layer of matrix, wherein the antibodies are covalently attached to the matrix and the matrix may be covalently attached to the device. Applicants traverse this rejection for the following reasons.

The antibodies taught by Kutryk are not "modified proteins" and they are not attached to a metal surface even via a cross-linker. The antibodies are cross-linked to a matrix. (Kutryk Abstract, Col. 12, lines 15-23). The matrix is "coated" onto the medical device as described in Kutryk, Column 10, lines 15-29. "The stent is dipped or sprayed with a liquid solution of the matrix of moderate viscosity." *Id.*

In Applicants' claims, "the modified protein is covalently bound to the metal surface" and this may be effected "through a thiol residue and a linker." (paragraph [0016] of Applicants' published application, US 2007/0092489. All further citations to paragraph numbers herein refer to the published application.) The Office Action states that "the limitation 'modified protein is covalently bound to the metal surface' recited in claim 1 does not require the amino acid residue of the modified protein directly forms a covalent bond in the absence of a cross-linker/coupling agent." (Office Action, page 11). However, this interpretation is incorrect. The

surface of the metal device is modified with a surface modifer that chemically coordinates with the metal surface. (Paragraphs [0041] - [0044]). Through the process of chemical coordination, the surface modifier reacts with the metals of the metal surface. Thus, unlike the invention of Kutryk, the modified protein is covalently bound to the reactive groups of the surface modifier, which is an integral part of the metal surface, and is not a coating. Therefore, the modified protein is "covalently bound to the metal surface" and not to a cross-linking or coupling agent.

For this reason, Kutryk does not disclose a composition comprising a metal surface and a modified protein, wherein the modified protein is covalently bound to the metal surface. Therefore, Kutryk does not anticipate claims 1, 8-10, or 33.

On the basis of the preceding discussion, Applicants respectfully request that the Section 102 rejections of claims 1, 8-10, and 33 be withdrawn.

Claims 1, 3, and 34 stand rejected under 35 USC Section 103(a) as unpatentable over Kutryk in view of Xu (US 7,001,745). Applicants traverse this rejection for the following reasons. As discussed above, Kutryk does not disclose a composition comprising a metal surface and a modified protein, wherein the modified protein is covalently bound to the metal surface. As stated in the Office Action, Xu discloses intein-mediated peptide ligation to generate a fusion protein. However, Xu does not disclose a composition comprising a metal surface and a modified protein, wherein the modified protein is covalently bound to the metal surface. Because Xu cannot compensate for the elements missing in Kutryk, Xu and Kutryk, alone or in combination, do not render claims 1, 3, or 34 unpatentable.

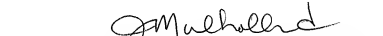
Claims 1, 33, and 35-37 stand rejected under 35 USC Section 103(a) as unpatentable over Kutryk in view of Li (US 6,524,572). Applicants traverse this rejection for the following reasons. As discussed above, Kutryk does not disclose a composition comprising a metal surface and a modified protein, wherein the modified protein is covalently bound to the metal

surface. The Office Action states that Li discloses a fusion protein comprising the extracellular domain of CAR/Hinge/protein A ligand for protein targeting. However, Li does not disclose a composition comprising a metal surface and a modified protein, wherein the modified protein is covalently bound to the metal surface. Because Li cannot compensate for the elements missing in Kutryk, Li and Kutryk, alone or in combination, do not render claims 1, 3, or 34 obvious.

Conclusion

For these reasons, it is respectfully submitted that the claims are in condition for immediate allowance and a notice to this effect is solicited. The Examiner is invited to telephone Applicants' attorney if it is believed that a telephonic interview would expedite prosecution of the application.

Respectfully submitted,



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